

### REMARKS

Claims 1-7, 17-28, and 30 are pending in the present case. Claims 1-7 stand rejected under 35 U.S.C. § 101. Claims 1-7, 17-28, and 30 stand rejected under 35 U.S.C. § 112, first paragraph and claim 27 stands rejected under 35 U.S.C. § 112, second paragraph. Claims 1-5, 17-20, 23-26, and 30 stand rejected under 35 U.S.C. § 102(b). Each of these rejections is addressed below.

### Amendments

Claim 1 (from which claims 2-7 depend), claim 17 (from which claims 18-25, 27, and 28 depend), and claim 30 have been amended to include an isolated nematode persistently infected with an isolated bacterium. Support for these amendments is found throughout the specification. No new matter has been added by any of these amendments.

### Rejections under 35 U.S.C. § 101

Claims 1-7 stand rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. In maintaining this rejection, the Office asserts that the claims encompass a product of nature which is not man-made. Applicants respectfully disagree for the reasons discussed below.

Turning first to the Office's assertion that the claimed product is not man-made, Applicants direct the Examiner's attention to page 6 of the specification which clearly

defines an “isolated nematode” as a “nematode that is *purified* from contaminating organisms and *maintained in a culture*.” Applicants assert that nematodes are *never* found in this form in nature. The only time a nematode is found in culture, as is claimed, is following human intervention. Furthermore, although the Office states that “nematode pathogens exist in nature and are capable of infecting nematodes,” Applicants submit that the relationship existing between the host nematode and the bacterium having the ability to establish a persistent infection, is a purely *artificial* relationship, and that occurs only with the help of a man’s hands. Such an interaction is not expected to exist on its own in nature and, at least to Applicants’ knowledge, has never been previously reported.

In sum, the claimed nematodes, being maintained in culture and being persistently infected, do not occur in nature and are clearly the result of human manipulation. Accordingly, the rejection under § 101 should be withdrawn.

#### Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-7, 17-28, and 30 stand rejected under 35 U.S.C. § 112, first paragraph as lacking an adequate written description. Claims 1-7, 17-28, and 30 further stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Each of these rejections is addressed below.

*Written Description*

*Claims 1-2, 4-7, 17-22, 24-28, and 30*

Claims 1-2, 4-7, 17-22, 24-28, and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description. Specifically, the Office asserts that the specification has failed to provide a description of nematodes, other than *C. elegans*, that can be persistently infected with a pathogen. Applicants respectfully traverse this rejection.

Applicants direct the Office's attention to the written description guidelines that state:

There may be situations where one species adequately supports a genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a representative number" depends on whether one skilled in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.<sup>1</sup>

Such a situation is presented here. At the time the present application was filed, numerous nematodes were known in the art and the level of knowledge was high. Indeed, as Applicants' have noted previously, the classification of the thousands of nematode species that have been described is largely based on morphology (e.g., structural features), life history, and habitat. Nematodes are simply roundworms, and therefore were well known to those skilled in the art at the time of filing. Accordingly, knowledge of the characteristics of *one* species of nematode conveys a considerable amount of

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<sup>1</sup> Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112 First Paragraph, "Written Description" Requirement Federal Register Vol. 66, No.4, p 1099-1111, Footnote 54.

information about other nematodes in the same taxonomic grouping. Thus, given that the level of knowledge in the art was high, the number of species necessary to satisfy the requirement of a representative number is low. Furthermore, given that nematodes, as a taxonomic group, possess common attributes, one skilled in the art would recognize members of the genus in view of the disclosure of *C. elegans*.

Applicants further submit that, in this case, the disclosure of a single species, *C. elegans*, fulfills the “representative number” requirement. Here, Applicants note that the Examination Guidelines cites *In re Rasmussen* 650 F.2d 212, 211 USPQ 323 (CCPA 1981) as an example of a situation in which a single species was deemed to be a representative number:

Disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to “adheringly applying” because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered.

Given that only one species was disclosed (as is asserted by the Examiner in the present Office action), the facts in the present case are similar to those in *Rasmussen*. Thus, the disclosure of a single species, namely *C. elegans*, is sufficient to satisfy the written description requirement.

Here, Applicants disclose methods and compositions directed to nematodes persistently infected with bacteria. To meet the “written description” standards, Applicants are only required to communicate to those skilled in the art that the claimed subject matter is intended to be part of their invention. Applicants have satisfied this

requirement since one skilled in the art reading the present specification would immediately understand that virtually *any* nematode might be employed according to the invention. In view of the foregoing arguments, Applicants respectfully request that this rejection be withdrawn.

*Claims 1-5, 17-20, 23-28, and 30*

Claims 1-5, 17-20, 23-28, and 30 also stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification. The Office maintains the rejection based on the assertion that the specification fails “to provide a description for pathogens other than bacteria embraced by the claims.” As amended, the rejected claims are now directed to nematodes persistently infected with bacteria (page 4, lines 15-23 of the specification), which the Office has acknowledged to be adequately described. This rejection may therefore be withdrawn.

*Claim 26*

Claim 26 also stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification. Applicants have cancelled claim 26, therefore rendering this rejection moot.

*Enablement*

Claims 1-7, 17-28, and 30 stand rejected under 35 U.S.C. § 112, first paragraph,

for lack of enablement. More specifically, the Office asserts that the specification, while being enabling for “a *C. elegans* persistently infected with a bacterium and methods of using the same to screen for compounds, is not enabling for all other nematodes and pathogens.”

As a preliminary matter, Applicants note that the claims, as amended, are now limited to nematodes persistently infected with a bacterium, rather than a pathogen. Because the Office has found this limitation to be enabling, this aspect of the rejection may be withdrawn.

Turning to the Office’s assertion that the invention is not enabled for nematodes other than *C. elegans*, Applicants respectfully disagree and point out that, at the time of filing, one skilled in the art could have readily practiced the claimed invention without undue experimentation, based on the teachings of the specification. As evidence of this assertion, Applicants direct the Examiner’s attention to the specification where various methods useful for generating nematodes persistently infected with bacteria are taught (see, for example, page 11, line 7 through page 13, line 22 and page 20, line 10 through page 23, line 1). The specification also provides ample guidance for screening methods that employ such nematodes for the identification of virulence factors (e.g., page 23, line 2 through page 25, line 14) and compounds that inhibit persistent infections (see, for example, page 25, line 15 through page 30, line 4).

As is stated previously, one skilled in the art reading the specification would immediately recognize that, in addition to *C. elegans*, virtually *any* nematode may be

employed according to the methods of the invention. One skilled in the art would also understand that the practice of the claimed invention would merely require standard application of routine methods, as described and exemplified in Applicants' specification.

Accordingly, one skilled in the art would understand that the practice of the invention would only require one to culture a nematode in the presence of a bacterium and assay for persistent infection, as is taught in the specification without undue experimentation. Thus, Applicants submit that the present specification enables the currently claimed methods and provides guidance to those skilled in the art on how to carry out the claimed invention. This basis for the rejection should therefore be withdrawn.

Applicants finally note that the Office, in maintaining this rejection, has again failed to provide support for doubting the inaccuracy of the present disclosure. Because Applicants have provided extensive teachings enabling the claimed invention throughout the specification, the burden is on the Examiner to provide evidence or reasoning to the contrary. This burden is set forth in the Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, "Enablement" requirement, which states:

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, *unless there is a reason to doubt the objective truth* of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts

the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.” 439 F.2d at 224, 169 USPQ at 370 (Emphasis added).

Because the Office has failed to meet this burden, Applicants submit that claims 1-7, 17-28, and 30 are enabled by the specification and respectfully request that the § 112, first paragraph rejection be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 27 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite. In particular, claim 27 was rejected for lack of antecedent basis for the phrase “inhibition of pathogenicity.” As amended, claim 17 no longer contains this phrase, and this rejection is now moot.

Rejections under 35 U.S.C. § 102(b)

Claims 1-5 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Tan et al. (PNAS, 1999, 96:2408-2413; hereinafter “Tan”). Claims 1-5, 17-20, 23-26, and 30 also stand rejected under 35 U.S.C. § 102(b) as being anticipated by Ausubel et al. (1998, WO 98/50080; hereinafter “Ausubel”). Applicants respectfully traverse this rejection.

The present claims are directed to compositions and screening methods that include nematodes persistently infected with bacteria. Applicants provide at pages 5-6 of the present specification at least two tests to assay for persistent infections:



By “persistent infection” or “persistently infected” is meant an invasion or colonization of a host animal (e.g., nematode) by a pathogen (e.g., *Salmonella*) that is damaging to the host, where *the size of the persistent pathogenic population that are associated with the host after the host has been transferred to a non-infectious environment remains at least 30%, preferably 50%, more preferably 80%, and most preferably 90%, or even 95% to 99% of the size of the pathogenic population before the transfer of the host to a non-infectious environment.* Such an infection also includes *an increase in the numbers of the pathogenic population that are associated with the host when the host is first exposed to a relatively small number of the pathogen mixed with an excess of non-pathogenic bacteria after which the host is transferred to a non-infectious environment.* A persistent infection is typically measured using a nematode feeding assay (as described herein) where bacteria are assayed for their ability to establish a long-lasting association in the worm intestine. (Emphasis added).

One such test is described, for example, at page 11, line 23 through page 12, line 17 of the specification. *C. elegans* (host) was fed with *Salmonella typhimurium* (*S. typhimurium*, pathogen) for a time period ranging between one to five hours and next transferred to plates containing *Escherichia coli* (*E. coli*). In spite of the transfer to a non-infectious environment, the rate of *C. elegans* killing was similar to that obtained when *C. elegans* was cultured in the constant presence of *S. typhimurium*. Based on the equal rate of killing in both groups, *S. typhimurium* is identified as having the ability to establish a persistent infection, as the size of the pathogenic population that is associated with the host after the host has been transferred to a non-infectious environment is assumed to be similar to the size of the pathogenic population prior to the transfer.

Turning to the cited references, both Tan and Ausubel, as is acknowledged by the Office, only go so far as to disclose *C. elegans* infected with *Pseudomonas aeruginosa*. *P. aeruginosa*, however, fails to *persistently* infect nematodes. Applicants, in the

specification, describe an experiment at page 12, lines 12-17 in which *C. elegans* was fed with *P. aeruginosa* for six hours and was subsequently transferred to an *E. coli* lawn. No *C. elegans* killing was observed within 60 hours or within the normal time frame required for 100% killing by constant feeding on *Pseudomonas aeruginosa*. Indeed, at page 19, line 21 of the specification, Applicants state: “A major difference between the *P. aeruginosa* and *S. typhimurium* infection models is that a small inoculum of *S. typhimurium* can proliferate in the intestine of *C. elegans* and establish a persistent and lethal infection even in the presence of a large excess of *E. coli* cells...” (Emphasis added). Tan and Ausubel simply do not describe Applicants’ claimed nematodes or methods of using such persistently infected nematodes. These references therefore cannot anticipate the presently claimed invention. Applicants therefore respectfully request that the § 102 rejection be withdrawn.

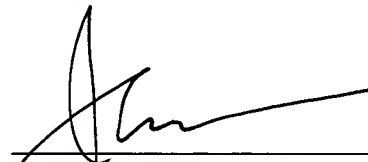
CONCLUSION

Applicants request reconsideration of the present rejections and allowance of claims 1-7, 17-28, and 30.

Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including June 18, 2004, and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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